REMARKS

Claims 1 and 53-56 and 58-77 are now pending. Claims 57 has been deleted without prejudice or disclaimer. Claim 55 has been amended to change the dependency from claim 1 to claim 54 so that it now contains proper antecedent basis for the phrase "biotin ligase." Claims 59-60 have been added to recite the full names of DEBS and the 6-dEB protein expressed therefrom. Claims 58 and 66 have been amended to correct minor typographical errors. Claim 61 has been amended to define more clearly that the *matB* gene is added. Support for this amendment is found, for example, in the paragraph bridging pages 5-6 and on page 7, line 19 of the present specification. Claim 61-63 and 69-71 have been amended to indicate that the *mat* gene is derived from *Streptomyces coelicolor* or *Rhizobium trifoli* support for this amendment is found for example on page 5, lines 28-30 and page 6, lines 14-15 of the present application.

The applicants gratefully acknowledge the Examiner's indication that the objections to claims 4-5, 8, and 9 under 37 C.F.R. § 1.75(c) have been withdrawn.

Election

Method claims 75-77 have been withdrawn from consideration. As these claims ultimately depended from claim 1, it is respectfully submitted that these method claims be rejoined in accordance with MPEP §804.21 upon allowance of claim 1.

Objection to the Specification

The title has been amended to more closely reflect the claim language as suggested by the Office. Therefore, the objection to the specification has been addressed, and the objection should be withdrawn.

Claim Objections

Claims 58 and 66 to which the Office objects have been amended such that these objections are moot. The applicants therefore request that the objection to these claims be withdrawn.

Claim Rejections Under 35 U.S.C. § 112, Second Paragraph

The applicants gratefully acknowledge the Examiner's indication that the various rejections to claims 1-9, 24-29, 42-43 under 35 U.S.C. § 112, second paragraph which were made in the previous Office action, have been withdrawn.

Claim 55 is rejected under 35 U.S.C. § 112, second paragraph, as being allegedly indefinite with regard to the phrase "the expression system for biotin ligase". Applicants have changed the dependency of this claim from claim 1 to claim 54 as suggested by the Examiner such that this claim contains proper antecedent basis.

Claim 57 is rejected under 35 U.S.C. § 112, second paragraph, as being allegedly indefinite with regard to the phrase "has no functional endogenous pathway for propionate catabolism". This claim has been deleted such that this rejection is now moot.

Claims 59, 60, 67, 68, 73 and 74 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter with regard to use of the abbreviations "DEBS" and "6-dEB." Claims 59 and 60 have been amended to include the definition in each of the claims where these terms are first used.

Thus, these rejections may be properly withdrawn.

Claim Rejections Under 35 U.S.C. § 112, First Paragraph

1) Written Description

The applicants gratefully acknowledge the Examiner's indication that the rejection to claims 1-9, 24-29, 42-43 (except with respect to the genus of phosphopantetheinyl transferases in claim 1) under 35 U.S.C. § 112, first paragraph (written description) has been withdrawn.

Claims 61, 64-69, and 72-74 are rejected under 35 U.S.C. §112, first paragraph, written description as allegedly adding new matter, and under 35 U.S.C. § 132 as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. These rejections are traversed. As mentioned in the Response filed August 7, 2002, support for a modification using only the *mat*B gene is found, for example, on page 6, lines 3-4 and on page 7, lines 2-7. It is not clear why the Office does not take this disclosure at face value to show that *mat*B may be used alone. Contrary to the Office's assertion that all descriptions of this operon describe either the entire *mat*ABC operon or the *mat*BC operon, it is respectfully submitted that there is no indication in the portions of the specification described immediately above that *mat*B must be used with genes encoding other proteins. Thus, it is respectfully submitted that a *prima facie* case of a lack of written description has not been established and no new matter has been added to the present claims.

The rejection of claims 1 and 53-74 under 35 U.S.C. §112, first paragraph, written description, as allegedly containing expression systems that are defined solely by function and without any structural limitations is traversed and reconsideration is respectfully requested. Each of the expression systems to which the Office objected are discussed below individually.

Regarding propionyl CoA carboxylase (pcc), the Office alleges that a "single example of a propionyl CoA carboxylase expression system is described in the instant specification, namely *pccB* and *accA2* from *S. coelicolor*". However, on page 7, lines 18-19, the present specification refers to such pcc genes as well as "their homologs in other organisms." Attached herewith is an article, Samols *et al.*, J. Biol. Chem. 263:14, 6461-6464 (1988), describing the molecular structure and homology among biotin-dependent carboxylases. In particular, rat pcc and human pcc are among the enzymes that are compared. This article notes that "[s]equence conservation over large evolutionary distances ...is not confined to the region surrounding the biotinyl lysine" which is highly conserved among these enzymes (please see Samols at 6463). It also acknowledges differences *e.g.,* between pcc and other enzymes based on function. *Id.* Thus, it is

respectfully submitted that a skilled artisan would understand that the applicants were in possession of a host cell that contained a broader range of pcc genes in other organisms than merely the *pccB* and *accA2* from *S. coelicolor* as mentioned by the office.

Regarding phosphopantetheinyl transferase, page 5 lines 14-16 of the present description described genes encoding these transferases which have been cloned. In this discussion, the present description refers to U.S. application number 08/728,742, which has been published as Canadian application 2,232,230, which was incorporated in the specification by reference. A copy of the PCT counterpart of this application (WO 97/13845) is submitted herewith. Unlike the Office's assertion that "the specification describes a single species, *sfp* from *B. subtilis*", this publication describes for instance, the sequence alignment/homology of the P-pant transferase enzyme superfamily and thus provides the structural relationship among the species in the genus of phosphopantetheinyl transferases. Thus, it is respectfully submitted that there is sufficient written description such that a skilled artisan would understand that the inventors has possession of the claimed invention with respect to phosphopantetheinyl transferase.

Regarding claim 54 and biotin ligase, similarly, it is respectfully submitted that a skilled artisan would understand that the applicants had possession of the genus of biotin ligases and not merely the species of *birA* from *E. coli* to which the Office refers in the action. A skilled artisan would understand that biotin ligase is needed, for example, for fatty acid synthesis and as such, is normally present in cells. The Samols article cited above, enumerates several organisms in which biotin ligase is present by virtue of its action in biotinylating various proteins described therein. Indeed, this assertion is supported by another article, Reche, P., *Protein Science,* 1922-1929 (2000), which states that "[c]ounterparts of the *E. coli* BirA [has] been previously identified in many organisms." Therefore, a skilled artisan would understand that the *E. coli birA* gene is not the only gene that encodes biotin ligases of which applicants had possession.

Regarding malonyl CoA enzymes, claims 61-62 and 69-70 have been amended to include the *mat*B gene or *mat*C gene from *Streptomyces coelicolor* or *Rhizobium trifoli.* Claims 63-71 have been amended to include the *mat*A gene from *Rhizobium trifoli.* As acknowledged by the

Office on page 11 last line of the action, the examples provide written description of these genes.

Therefore, all concerns with regard to written description have been addressed and withdrawal of this rejection is requested.

2) Enablement

Claims 1, 53, and 56-60 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly not providing enablement for host cells expressing propionyl CoA carboxylase in the absence of coexpressing biotin ligase. This rejection is traversed. It is respectfully submitted that there is nothing in the present application that states that the *host cells* cannot be made without an expression system for biotin ligase. To the contrary, although the specification discloses that "biotin ligase is needed for *activation* of these [pcc] *proteins* (emphasis added)," there is no disclosure suggesting that the host cells cannot be made without the addition of a *gene* for expressing a biotin ligase protein. As mentioned above, biotin ligase is produced by most organisms, and thus, biotin ligase need not be included in an expression system added to a host cell. Also, there is no discussion in the present application that biotin ligase must be expressed by the cell. The disclosure does not eliminate the possibility that biotin ligase, for example, may be added to a culture medium for expressing the host cells to activate the proteins. Therefore, it is respectfully submitted that in order to make the claimed host cell, an expression for biotin ligase need not be present and thus the scope of the present claims is properly enabled by the present specification.

Claim 57 is rejected under 35 U.S.C. § 112, first paragraph, scope of enablement. Deletion of this claim renders moot this rejection.

Withdrawal of these rejections is respectfully requested.

Claim Rejection Under 35 U.S.C. § 102

The applicants gratefully acknowledge the Examiner's indication that all of the anticipation rejections made in the previous Office action have been withdrawn. Applicants gratefully acknowledge that claims 1, 53-56, 58-60, 66 and 69-74 are free of art.

The rejection of claims 61-65 and 67-68 under 35 U.S.C. § 102(b) as being anticipated by Kao *et al.* is traversed and reconsideration is respectfully requested. The Office appears to allege that due to the presence of an endogenous *matB* gene in *S. coelicolor*, claim 61 is anticipated by any recombinant *Streptomyces* host cell. However, claim 61 specifically refers to a genetic modification which incorporates a *matB* gene which enhances the synthesis of the polyketide. Such modification is not disclosed or suggested in Kao, and thus it is respectfully submitted that *prima facie* anticipation has not been established. Nonetheless, in order more clearly to define the *matB* gene without limiting the scope of the claim and to facilitate allowance of the present claims, claim 61 has been amended to define this gene as an added *matB* gene to distinguish it from a *Streptomyces matB* gene that may be present in the cell before such gene is incorporated. As such, it is respectfully submitted that this claim is not anticipated by the Kao reference. Withdrawal of this rejection, therefore, is respectfully requested.

CONCLUSION

The claims have proper written description basis in the present specification because homologs of the expression systems in question as disclosed in the present specification are known in the art and thus need not be enumerated in the specification. Claims 1, 53 and 56-60 are properly enabled because there is no requirement that an expression system for biotin ligase be present in the host cell. Finally, Kao does not anticipate claims 61-65 and 67-68 as Kao does not teach genetically modifying a *Streptomyces* host cell with the incorporation of a *matB* gene.

Thus, it is respectfully submitted that the present claims are in condition for allowance and such action is respectfully requested. If the Examiner does not believe that the present claims are in condition for allowance, she is kindly requested to telephone the undersigned.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, Applicant petitions for any required relief including extensions of time and authorizes the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. 286002001100.

Respectfully submitted,

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